HIGH PRODUCTION VOLUME (HPV)

CHALLENGE PROGRAM

FINAL SUBMISSION

For

Benzoic Acid, 2-Hydroxy-, Mono-C14-18 Alkyl Derivatives, Calcium Salts

Prepared by
The American Chemistry Council
Petroleum Additives Panel
Health, Environmental and Regulatory Task Group

December 2006

LIST OF MEMBER COMPANIES IN THE
HEALTH, ENVIRONMENTAL AND REGULATORY TASK GROUP

The Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council Petroleum Additives Panel include the following member companies:

Afton Chemical Corporation (formerly Ethyl Corporation)

Chevron Oronite Company, LLC

Infineum

The Lubrizol Corporation

EXECUTIVE SUMMARY

The Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council submits for review and public comment this final submission dossier for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts (CAS Number 114959-46-5) to the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program.

Fate and Transport Characteristics. Based on the physicochemical properties and molecular structure, the HERTG concluded that benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts is most likely to partition to soils and sediments. The HERTG calculated fugacity data on benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts. Since this material lacks any readily hydrolyzable moieties, hydrolysis modeling was not conducted. Benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts was subjected to biodegradability testing and found to be poorly biodegradable. The HERTG developed computer modeled data that indicated benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts does not possess the potential to photodegrade.

Aquatic Toxicology. Data on acute fish toxicity, acute invertebrate toxicity, and algal toxicity were reviewed. The findings of the available studies indicated benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts possesses low acute toxicity to fish, aquatic invertebrates, and algae.

Mammalian Toxicology - Acute. Data on acute mammalian toxicity (oral and dermal) were reviewed. Oral and dermal LD_{50} levels for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts were very high, indicating essentially no toxicity.

Mammalian Toxicology - Subchronic Toxicity. The HERTG completed a repeated-dose study for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts. After administration of benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts to rats, the liver and kidneys were mildly affected at the highest dose. However, since the significant effects were both mild and only observed at highest dose, benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts possesses a low order of repeated-dose toxicity to mammals.

Mammalian Toxicology - Reproductive and Developmental Toxicity. The HERTG investigated the reproductive and developmental toxicity of benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts. Exposure to benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts did not impact fertility or reproduction in rats. Additionally, this material did not cause any developmental effects in offspring, thus indicating benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts dose not cause reproductive or developmental toxicity.

Mammalian Toxicology - Mutagenicity. Bacterial reverse mutation assay data was available for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts and the results were negative, both with and without metabolic activation. Benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts was also tested in an *in vitro* chromosomal aberration assay. The results were negative for clastogenicity, both with and without metabolic activation.

Conclusion. Based on the available data and the physiochemical, environmental fate, aquatic toxicology, and mammalian toxicology studies conducted for this submission, benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts possesses minimal toxicity to aquatic organisms or mammals. As this final submission was completed, the HERTG carefully evaluated the number of animals necessary for testing and the conditions to which animals might be exposed. Thus, a minimal amount of testing involving the use of animals was employed.

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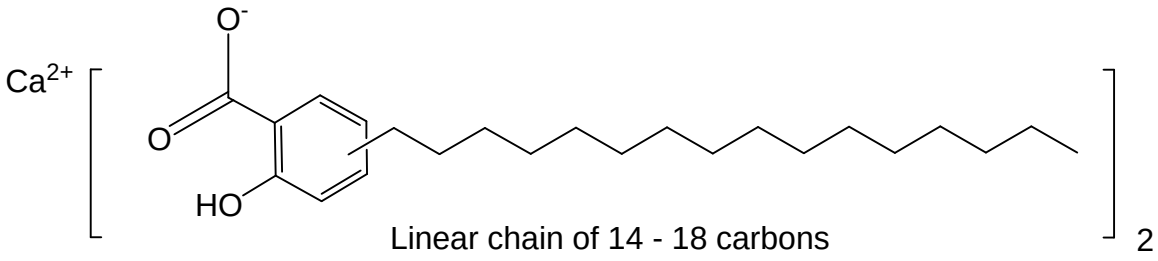
1.0 INTRODUCTION

In March 1999, the Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG) of the American Chemistry Council committed to address data needs for certain chemicals listed under the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program. This final submission follows up on that commitment and specifically, how the HERTG fulfilled the Screening Information Data Sets (SIDS) requirements for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts (CAS No.: 114959-46-5; structure shown in Figure 1).

FIGURE 1. CHEMICAL STRUCTURE OF BENZOIC ACID, 2-HYDROXY-, MONO-C14-18 ALKYL DERIVATIVES, CALCIUM SALTS



Benzoic acid, 2-hydroxy-,mono-C14-18 alkyl derivatives, calcium salts
CAS # 114959-46-5

In preparing this final submission the following steps were undertaken:

> Step 1: A review of the literature and confidential company data was conducted on the physicochemical properties, mammalian toxicity endpoints, and environmental fate and effects for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts, using its CAS number, CAS name, and synonyms. Searches included the following sources: MEDLINE, BIOSIS, CANCERLIT, CAPLUS, CHEMLIST, EMBASE, HSDB, RTECS, EMIC, and TOXLINE databases; the TSCATS database for relevant unpublished studies on these chemicals; and standard handbooks and databases (e.g., Sax, CRC Handbook on Chemicals, IUCLID, Merck Index, and other references) for physicochemical properties.
>
> Step 2: The compiled data was evaluated for adequacy in accordance with the EPA guidance documentation. Where additional data was needed, testing was completed to meet the SIDS requirements.

Testing was conducted using two formulations of benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts. One formulation was 43% benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts, 48% highly refined lubricating base oil and 9% inorganic calcium salts; this formulation will be referred to in the final submission as “AI-43”. The second formulation was 28% benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts, 51% highly refined

lubricating base oil and 21% inorganic calcium salts; this formulation will be referred to in the final submission as “AI-28”.

2.0 USE INFORMATION

In the general discussion of use and exposure, the material will be referred to as calcium alkyl salicylates. Calcium alkyl salicylates are detergent additives used in gasoline and diesel engine oils, for both crankcase and marine applications. Additional functionality includes excess basicity for neutralisation of acids, detergency to assist in keeping carbon particles (soot) in suspension and minimising sludge formation, and to act as anti-oxidant and anti-rust preventative agents.

3.0 PHYSICOCHEMICAL PROPERTIES

The physiochemical properties of benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts are shown in Table 1, below.

TABLE 1. PHYSIOCHEMICAL PROPERTIES OF BENZOIC ACID, 2-HYDROXY-, MONO-C14-18 ALKYL DERIVATIVES, CALCIUM SALTS

Physical/Chemical Characteristics	**Study Results**
Melting Point	Not Applicable
Boiling Point	310 ^{o} C
Vapor Pressure	1.68 x 10^{-9} mm Hg @ 25^{o} C [1]
Partition Coefficient	> 3.9 (AI-43)
Water Solubility	9 - 103 mg/L at 20^{o}C (multiple studies for AI-28 & AI – 43)

[1] Modeled value using EpiWin version 3.12 software

4.0 ENVIRONMENTAL FATE DATA

4.1 Biodegradability

Biodegradation data (OECD 301B) was available for AI-43, with biodegradation of 39% after 28 days and 63% after 56 days. The results indicate that this material is not readily biodegradable. The data was considered adequate and reliable and as a result, additional biodegradation testing was not conducted.

4.2 Hydrolysis

No published or unpublished hydrolysis studies were located for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts. However, benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts does not contain any readily hydrolysable functional groups. Therefore, no hydrolysis testing was conducted.

4.3 Photodegradation

No published or unpublished photodegradation studies were located for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts. As a result, photodegradation was estimated using AOPWIN software. The results as shown in Table 2, indicate that benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts is not likely to undergo photodegradation.

4.4 Fugacity Modeling

No published or unpublished fugacity-based multimedia fate modeling data were located for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts. As a result, the fugacity was estimated using EPIWIN, version 3.12. The results (shown in Table 2) indicate benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts is likely to partition primarily to soils and sediments.

TABLE 2. ENVIRONMENTAL FATE DATA FOR BENZOIC ACID, 2-HYDROXY-, MONO-C14-18 ALKYL DERIVATIVES, CALCIUM SALTS

Environmental Fate	Study Results
Biodegradation	39 % after 28 days for AI-43 (OECD 301B)
Photodegradation[1]	AOPWIN Model Estimation OH- Rate Constant (cm3/molec-sec) = 36.53×10^{-12} Half-life = 0.29 days
Fugacity[1]	Mass distribution (%) Air 0.23 Water 3.73 Soil 28.2 Sediment 67.8

[1] Modeled values using EpiWin version 3.12 and using water solubility of 9 mg/L and boiling point of 310^{o} C.

5.0 ECOTOXICOLOGY DATA

5.1 Acute Fish Toxicity

An acute fish toxicity study was available for benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts (AI-28) and the 96 hour LC_{50} of for rainbow trout (*Pimephales promelas*) was > 1000 mg/L and the no observed effect concentration (NOEC) was 1000 mg/L.

5.2 Acute Invertebrate Toxicity

Multiple acute invertebrate studies were available for AI-28 and AI-43. In an acute *Daphnia magna* toxicity study with AI-43, 100% immobilization occurred at ≥100 mg/L (WAF) after 48 hours and at 1000 mg/L after 24 hours. The no observed effect level was 10 mg/L (WAF). Therefore, the 48 hour EL50 was between 10 and 100 mg/L. In an acute *Daphnia magna* toxicity study with AI-28, no immobilizations were observed using WAF preparations of 0, 100, 220, 460 and 1000 mg/L. Therefore, the 48 hour EL50 was >1000 mg/L and the NOEC was 1000 mg/L.

5.3 Algal Growth Inhibition

In an available algal growth inhibition study, the 48-96 hour EL50 of AI-43 in freshwater algae (*Pseudokirchneriella subcapitata*) was > 1000 mg/L (WAF). The 0-72 hour EL50 of AI-28 in freshwater algae (*Pseudokirchneriella subcapitata*) was > 1000 mg/L (WAF).

TABLE 3. AQUATIC TOXICITY DATA FOR BENZOIC ACID, 2-HYDROXY-, MONO-C14-18 ALKYL DERIVATIVES, CALCIUM SALTS

Ecotoxicity study	Study Results	
	AI – 43	AI – 28
Acute Toxicity to Fish	No Data Located	96 hour LL50: >1000 mg/L (WAF) 96 hour NOEC = 1000 mg/L (WAF)
Acute Toxicity to Invertebrates (*Daphnia magna*)	48 hour EL50 : between 10-100 mg/L, 100% immobilization at ≥ 100 mg/L (WAF); NOEL = 10 mg/L (WAF)	48 hour EL50: > 1000 mg/L (WAF) 48 hour NOEC = 1000 mg/L (WAF)
Acute Toxicity to Algae	48-96 hour EL50: > 1000 mg/L (WAF)	72 hour EL50 : > 1000 mg/L (WAF)

6.0 MAMMALIAN TOXICOLOGY DATA

6.1 Acute Mammalian Toxicity

Acute oral and dermal toxicity studies were available for AI-28. In these studies, the LD50s were greater than 5000 mg/kg by the oral route and greater than 2000 mg/kg by the dermal route indicating a low concern for toxicity.

6.2 Repeated Dose Toxicity

A repeat dose toxicity study (OECD 407) for AI-43 was conducted. Although the liver of males and females was affected at the highest doses (elevated serum alkaline phosphatase and alanine transferase activities and liver weights relative to body weights), this material did not cause significant toxicity to rats. (Table 4)

6.3 Reproductive and Developmental Toxicity

The HERTG conducted a reproductive and developmental screening study (OECD 421) in rats on AI-43. Administration of this material did not impact fertility or reproduction and did not cause developmental toxicity (Table 4).

TABLE 4. MAMMALIAN TOXICITY DATA FOR BENZOIC ACID, 2-HYDROXY-, MONO-C14-18 ALKYL DERIVATIVES, CALCIUM SALTS

Mammalian Toxicity	Study Results
Acute Toxicity	Oral LD_{50} > 5 g/kg Dermal LD_{50} > 2 g/kg
Repeat Dose Toxicity	<u>Oral gavage 28-day study in rats (OECD 407)</u> NOAEL = 150 mg/kg/day Significant findings: **500 mg/kg/day** - Liver weights relative to body weight values were statistically elevated in males and females as compared to controls. -Thyroid/parathyroid weights relative to body weights were statistically higher in males as compared to controls. -In males and females, serum alkaline phosphatase and alanine aminotransferase activity was significantly elevated relative to controls. -In males, prothrombin time and triglyceride levels were significantly elevated as compared to controls. **150 mg/kg/day** -No significant adverse effects. **50 mg/kg/day** -In males, significantly elevated triglyceride levels relative to controls.
Reproductive and Developmental	<u>Reproductive and developmental screen (OECD 421) –</u>

Toxicity	Oral gavage and rats Reproductive NOEC = 500 mg/kg/day (highest dose) Significant findings: Administration of AI-43 did not adversely impact fertility/reproduction in rats after administration of any dose (50, 150, or 500 mg/kg/day) Litter sizes, fertility indices, pup weights and pup survival were similar between controls and all dose groups. Additionally, administration of benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts did not cause any developmental toxicity effects at any dose.

7.0 GENETIC TOXICOLOGY DATA

7.1 Mutagenicity

Bacterial reverse mutation data was available for both AI -28 and AI-43. Both AI-43 and AI-28 were non-mutagenic in *Salmonella typhimurium* and *Escherichia coli* in vitro point mutation assays, in the presence and absence of metabolic activation.

7.2 Clastogenicity

A chromosomal aberration study (OECD 473) was conducted in human peripheral blood lymphocytes using AI-43. This material did not cause an increased rate of chromosomal aberrations or endoreduplication in the presence or absence of metabolic activation. Therefore, benzoic acid, 2-hydroxy-, mono-C14-18 alkyl derivatives, calcium salts was determined to be non-clastogenic.

TABLE 5. SUMMARY OF DATA FOR BENZOIC ACID, 2-HYDROXY-, MONO-C14-18 ALKYL DERIVATIVES, CALCIUM SALTS

CAS Number	Environmental Fate					Ecotoxicity		
	Physical Chem	Photodeg	Hydrolysis	Fugacity	Biodeg	Acute Fish Toxicity	Acute Invert Toxicity	Algal Toxicity
114959-46-5	A/C	C	D	C	A	A	A	A

CAS Number	Human Health Effects				
	Acute Toxicity	Point Mutations	Chrom Effects	Sub-chronic	Repro/ Develop
114959-46-5	A	A	A	A	A

A Adequate data available
C Computer modeling completed
D Technical discussion completed